PHYSICIANS' DESK REFERENCE®

Medical Consultant
Ronald Arky, MD, Charles S. Davidson Professor of Medicine and Master, Francis Weld Peabody Society, Harvard Medical School

President and Chief Operating Officer, Drug Information Services Group: Thomas F. Rice

Director of Product Management: Stephen B. Greenberg
Associate Product Managers: Cy S. Caine, Howard N. Kanter
National Sales Manager: James R. Pantaleo
Senior Account Manager: Michael S. Sarajian
Account Managers
Dikran N. Barsamian
Donald V. Bruccoleri
Lawrence C. Keary
Jeffrey M. Keller
P. Anthony Pinsonault
Anthony Sorce
Trade Sales Manager: Robin B. Bartlett
Trade Sales Account Executive: Bill Gaffney
Direct Marketing Manager: Robert W. Chapman
Marketing Communications Manager: Maryann Malorgio
Director, Professional Support Services: Mukesh Mehta, RPh
Drug Information Specialists: Thomas Fleming, RPh, Marion Gray, RPh
Editor, Special Projects: David W. Sifton

Vice President of Production: Steven R. Andreazza
Manager, Database Administration: Lynne Handler
Contracts and Support Services Director: Marjorie A. Duffy
Director of Production: Carrie Williams
Production Managers: Kimberly Hiller-Vivas, Tara L. Walsh
Production Coordinators: Amy B. Douma, Dawn B. McCall
Format Editors: Gregory J. Westley, Edna V. Berger
Index Editor: Jeffrey Schaefer
Art Associate: Joan K. Akerlind
Director of Corporate Communications: Gregory J. Thomas
Electronic Publishing Coordinator: Joanne M. Pearson
Electronic Publishing Designer: Kevin J. Leckner
Art Director: Richard A. Weinstock
Digital Photography: Shawn W. Cahill, Frank J. McElroy, III
Director, Circulation & Fulfillment: Marianne Clarke
Product Fulfillment Manager: Stephen Schweikhart

Officers of Medical Economics: President and Chief Executive Officer: Norman R. Snesil; President and Chief Operating Officer: Curtis B. Allen; Executive Vice President and Chief Financial Officer: J. Crispin Ashworth; Senior Vice President—Corporate Operations: John R. Ware; Senior Vice President—Corporate Business Development: Raymond M. Zoeller; Vice President, Information Services and Chief Information Officer: Edward J. Zecchini

ISBNs: 1-56363-152-0 and 1-56363-156-3

DISTA

For description of Dista Identi-Code® Identifications, see Dista Identi-Code Index beginning of Dista Product Information Section.

DISTA PRODUCTS P. 915

500 mg

Keftab®
(cephalexin HCl)

DISTA PRODUCTS P. 919

10 mg

Prozac®
(fluoxetine HCl)

DISTA PRODUCTS P. 919

20 mg

Prozac®
(fluoxetine HCl)

DUPONT PHARMA

®COUMADIN®, the COUMADIN color logo, COLORS OF COUMADIN, and the color and configuration of COUMADIN® tablets are trademarks of The DuPont Merck Pharmaceutical Company. Any unlicensed use of these trademarks is expressly prohibited under the U.S. Trademark Act.

DUPONT PHARMA P. 926

1 mg 2 mg

2 1/2 mg 4 mg 5 mg

7.5 mg 10 mg

†Coumadin®
(Warfarin Sodium Tablets, USP) Crystalline

DUPONT PHARMA P. 938

Percocet®
(oxycodone HCl/acetaminophen, USP)
5 mg / 325 mg

C-II DUPONT PHARMA P. 939

Percodan®
(oxycodone HCl, oxycodone terephthalate, aspirin, USP)
4.5 mg / 0.38 mg / 325 mg

RX DUPONT PHARMA P. 940

50 mg

REVIA™
(naltrexone HCl)

RX DUPONT PHARMA P. 943

647* 10 mg / 100 mg

650* 25 mg / 100 mg

654* 25 mg / 250 mg

Sinemet®
(Carbidopa-Levodopa)

RX DUPONT PHARMA P. 944

601* 25 mg / 100 mg

621* 50 mg / 200 mg

*Manufactured by Merck & Co., Inc. for DuPont Pharma.

Sinemet® CR
(Carbidopa-Levodopa)
Sustained-Release

ESI LEDERLE

RX ESI LEDERLE P. 974

894* 5 mg

Aygestin®
(norethindrone acetate, USP)

RX ESI LEDERLE P. 975

2.5 mg

5 mg

10 mg

Cyclin®
(medroxyprogesterone acetate tablets, USP)

RX ESI LEDERLE P. 976

435* 250 mg

437* 330 mg

†Grisactin® Ultra
(griseofulvin, ultramicrosize)

FOREST

RX FOREST PHARMACEUTICALS INC. P. 1005

250 mcg/per puff
7 g 100 metered inhalations

AEROBID® Inhaler System
(flunisolide)

RX FOREST PHARMACEUTICALS INC. P. 1005

250 mcg/per puff
7 g 100 metered inhalations

AEROBID®-M Inhaler System
(flunisolide)

RX FOREST PHARMACEUTICALS INC. P. 1007

AeroChamber® with Mask-Large

AeroChamber® with Mask-Small

AeroChamber®

RX FOREST PHARMACEUTICALS INC. P. 1010

Cervidil™ Vaginal Insert
(dinoprostone 10 mg)

RX FOREST PHARMACEUTICALS INC. P. 1013

535-12

Esgic®
(butalbital*, acetaminophen, caffeine)
50 mg / 325 mg / 40 mg
*(Warning: May be habit forming)

RX FOREST PHARMACEUTICALS INC. P. 1018

Esgic-plus™
(butalbital*, acetaminophen, caffeine)
50 mg / 500 mg / 40 mg
*(Warning: May be habit forming)

RX FOREST PHARMACEUTICALS INC. P. 1018

100 mg

Flumadine®
(rimantadine HCl)
23 mL
50 mg/5 mL

C-III FOREST PHARMACEUTICALS INC. P. 1018

Lorcet® 10/650
(hydrocodone bitartrate, acetaminophen)
10 mg/650 mg *(Warning: May be habit forming)

C-III FOREST PHARMACEUTICALS INC. P. 1018

Lorcet® Plus
(hydrocodone* bitartrate, acetaminophen)
7.5 mg/650 mg *(Warning: May be habit forming)

RX FOREST PHARMACEUTICALS INC. P. 1018

25 mcg 50 mcg 75 mcg

88 mcg 100 mcg 112 mcg

125 mcg 137 mcg 150 mcg

175 mcg 200 mcg 300 mcg

Levothroid®
(levothyroxine sodium)

RX FOREST PHARMACEUTICALS INC. P. 1020

100 mg

Tessalon®
(benzonatate)

RX FOREST PHARMACEUTICALS INC. P. 1009

1/4 g. 1/2 g. 1 g. 1 1/2 g.

2 g. 3 g.

1/4 g. 1/2 g. 1 g.

Armour® Thyroid
(thyroid USP)

RX FOREST PHARMACEUTICALS INC. P. 1020

1/4 1/2 1

Thyrolar®
(liotrix)

complications of sudden steroid

—Safe use of Nalfon during pregnancy not been established; therefore, administ- patients and nursing mothers is not duction studies have been performed in When fenoprofen was given to rats during ntinued until the time of labor, parturition similar results have been found with other inflammatory drugs that inhibit prosta-

—Fenoprofen calcium is not recom- in children because documented clinical ex- insufficient to establish safety and a suit- en in the pediatric age group.

ACTIONS

studies for rheumatoid arthritis, osteoarthri- oderate pain and studies of pharmacokinet- were compiled from a checklist of potential and the following data emerged. These rvations in 6,786 patients, including 188 ob- st 52 weeks. For comparison, data are also complaints received from the 266 patients placebo in these same trials. During short-term lgesia, the incidence of adverse reactions was r than that seen in longer-term studies.

GREATER THAN 1%

Relationship

—During clinical trials with Nalfon® lcium, USP), the most common adverse reac- intestinal in nature and occurred in 20.8% ving Nalfon as compared to 16.9% of pa- placebo. In descending order of frequency, included dyspepsia (10.3%, Nalfon, vs 2.3%, (7.7% vs 7.1%), constipation (7% vs 1.5%), % vs 1.9%), abdominal pain (2% vs 1.1%), and % vs 4.1%).

discontinued because of adverse gastrointesti- less than 2% of patients during premarket-

—The most frequent adverse neurologic headache (8.7% treated vs 7.5% placebo) and 5% vs 6.4%). Dizziness (6.5% vs 5.6%), tremor and confusion (1.4% vs none) were noted less

discontinued in less than 0.5% of patients be- side effects during premarketing studies.

—Increased sweating (4.6% vs 0.4%), % vs 0.8%), and rash (3.7% vs 0.4%) were re-

discontinued in about 1% of patients because of related to the skin during premarketing

—Tinnitus (4.5% vs 0.4%), blurred vision and decreased hearing (1.6% vs none) were

discontinued in less than 0.5% of patients be- adverse effects related to the special senses during studies.

—Palpitations (2.5% vs 0.4%).

discontinued in about 0.5% of patients because cardiovascular reactions during premarketing

—Nervousness (5.7% vs 1.5%), asthenia (5.4% peripheral edema (5.0% vs 0.4%), dyspnea (2.8% vs (1.7% vs 1.5%), upper respiratory infection 6%), and nasopharyngitis (1.2% vs none).

LESS THAN 1%

Causal Relationship

adverse reactions, occurring in less than 1% of reported in controlled clinical trials and vol- made since Nalfon® (Fenoprofen Calcium, initially marketed. The probability of a causal exists between Nalfon and these adverse reac-

—Gastritis, peptic ulcer with/without per- gastrointestinal hemorrhage, anorexia, flatulence, and blood in the stool. Increases in alkaline phos- and SGOT, jaundice, and cholestatic hepatitis (see Precautions).

Urinary Tract —Dysuria, cystitis, hematuria, oliguria, nephritis, interstitial nephritis, nephrosis, and papil- (see Warnings).

—Angioedema (angioneurotic edema).

—Purpura, bruising, hemorrhage, thrombocy- hemolytic anemia, aplastic anemia, agranulocyto- leukopenia.

—Anaphylaxis, urticaria, malaise, insomnia, tachycardia.

LESS THAN 1%

Relationship Unknown

reported either in clinical trials or spontane- occurred in circumstances in which a causal relation- could be established. However, with these rarely reported reactions, the possibility of such a relationship can- not be excluded. Therefore, these observations are listed to alert the physician.

Skin and Appendages —Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, and alopecia.

Digestive System —Aphthous ulcerations of the buccal mucosa, metallic taste, and pancreatitis.

Cardiovascular —Atrial fibrillation, pulmonary edema, electrocardiographic changes, and supraventricular tachycardia.

Nervous System —Depression, disorientation, seizures, and trigeminal neuralgia.

Special Senses —Burning tongue, diplopia, and optic neuritis.

Miscellaneous —Personality change, lymphadenopathy, mastodynia, and fever.

OVERDOSAGE

Signs and Symptoms —Symptoms of overdose appear within several hours and generally involve the gastrointestinal and central nervous systems. They include dyspepsia, nausea, vomiting, abdominal pain, dizziness, headache, ataxia, tinnitus, tremor, drowsiness, and confusion. Hyperpyrexia, tachycardia, hypotension, and acute renal failure may occur rarely following overdose. Respiratory depression and metabolic acidosis have also been reported following overdose with certain NSAIDs.

Treatment —To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the *Physicians' Desk Reference (PDR).* In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Alkalinization of the urine, forced diuresis, peritoneal dialysis, hemodialysis, and charcoal hemoperfusion do not enhance systemic drug elimination.

DOSAGE AND ADMINISTRATION

Analgesia —For the treatment of mild to moderate pain, the recommended dosage is 200 mg every 4 to 6 hours, as needed.

Rheumatoid Arthritis and Osteoarthritis —The suggested dosage is 300 to 600 mg, 3 or 4 times a day. The dose should be tailored to the needs of the patient and may be increased or decreased depending on the severity of the symptoms. Dosage adjustments may be made after initiation of drug therapy or during exacerbations of the disease. Total daily dosage should not exceed 3,200 mg.

If gastrointestinal complaints occur, Nalfon® (Fenoprofen Calcium, USP) may be administered with meals or with milk. Although the total amount absorbed is not affected, peak blood levels are delayed and diminished.

Patients with rheumatoid arthritis generally seem to require larger doses of Nalfon than do those with osteoarthritis. The smallest dose that yields acceptable control should be employed.

Although improvement may be seen in a few days in many patients, an additional 2 to 3 weeks may be required to gauge the full benefits of therapy.

HOW SUPPLIED

(℞) Pulvules:

200 mg* (white and ocher) (No. 415)—(Identi-Code† H76) (RxPak‡ of 100) NDC 0777-0876-02

300 mg* (yellow and ocher) (No. 416)—(Identi-Code† H77) (RxPak‡ of 100) NDC 0777-0877-02; (500s) NDC 0777-0877-03

(℞) Tablets (DISTA imprinted on one side, NALFON on other side):

600 mg* (yellow, paracapsule-shaped, scored) (No. 1900)—(RxPak‡ of 100) NDC 0777-2159-02; (500s) NDC 0777-2159-03

* Equivalent to fenoprofen.

† Identi-Code® (formula identification code, Dista).

‡ All RxPaks (prescription packages, Dista) have safey closures.

Store at controlled room temperature, 59° to 86°F (15° to 30°C).

[121390]

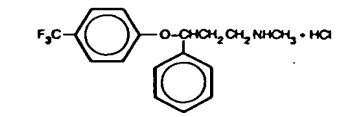
PROZAC® ℞

[*prō 'zăk*]

(fluoxetine hydrochloride)

DESCRIPTION

Prozac® (Fluoxetine Hydrochloride) is an antidepressant for oral administration; it is chemically unrelated to tricyclic, tetracyclic, or other available antidepressant agents. It is designated (±)-N-methyl-3-phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride and has the empirical formula of $C_{17}H_{18}F_3NO \cdot HCl$. Its molecular weight is 345.79. The structural formula is:



Fluoxetine hydrochloride is a white to off-white crystalline solid with a solubility of 14 mg/mL in water.

Each Pulvule® contains fluoxetine hydrochloride equivalent to 10 mg (32.3 μmol) or 20 mg (64.7 μmol) of fluoxetine. The Pulvules also contain F D & C Blue No. 1, gelatin, iron oxide, silicone, starch, titanium dioxide, and other inactive ingredients.

The oral solution contains fluoxetine hydrochloride equivalent to 20 mg/5 mL (64.7 μmol) of fluoxetine. It also contains alcohol 0.23%, benzoic acid, flavoring agent, glycerin, purified water, and sucrose.

CLINICAL PHARMACOLOGY

Pharmacodynamics —The antidepressant and antiobsessive-compulsive action of fluoxetine is presumed to be linked to its inhibition of CNS neuronal uptake of serotonin. Studies at clinically relevant doses in man have demonstrated that fluoxetine blocks the uptake of serotonin into human platelets. Studies in animals also suggest that fluoxetine is a much more potent uptake inhibitor of serotonin than of norepinephrine.

Antagonism of muscarinic, histaminergic, and α_1-adrenergic receptors has been hypothesized to be associated with various anticholinergic, sedative, and cardiovascular effects of classical tricyclic antidepressant drugs. Fluoxetine binds to these and other membrane receptors from brain tissue much less potently in vitro than do the tricyclic drugs.

Absorption, Distribution, Metabolism, and Excretion:

Systemic Bioavailability—In man, following a single oral 40 mg dose, peak plasma concentrations of fluoxetine from 15 to 55 ng/mL are observed after 6 to 8 hours.

The Pulvule and oral solution dosage forms of fluoxetine are bioequivalent. Food does not appear to affect the systemic bioavailability of fluoxetine, although it may delay its absorption inconsequentially. Thus, fluoxetine may be administered with or without food.

Protein Binding—Over the concentration range from 200 to 1,000 ng/mL, approximately 94.5% of fluoxetine is bound in vitro to human serum proteins, including albumin and α_1-glycoprotein. The interaction between fluoxetine and other highly protein-bound drugs has not been fully evaluated, but may be important (see Precautions).

Enantiomers—Fluoxetine is a racemic mixture (50/50) of *R*-fluoxetine and *S*-fluoxetine enantiomers. In animal models, both enantiomers are specific and potent serotonin uptake inhibitors with essentially equivalent pharmacologic activity. The *S*-fluoxetine enantiomer is eliminated more slowly and is the predominant enantiomer present in plasma at steady state.

Metabolism—Fluoxetine is extensively metabolized in the liver to norfluoxetine and a number of other, unidentified metabolites. The only identified active metabolite, norfluoxetine, is formed by demethylation of fluoxetine. In animal models, *S*-norfluoxetine is a potent and selective inhibitor of serotonin uptake and has activity essentially equivalent to *R*- or *S*-fluoxetine. *R*-norfluoxetine is significantly less potent than the parent drug in the inhibition of serotonin uptake. The primary route of elimination appears to be hepatic metabolism to inactive metabolites excreted by the kidney.

Clinical Issues Related to Metabolism/Elimination —The complexity of the metabolism of fluoxetine has several consequences that may potentially affect fluoxetine's clinical use.

Variability in Metabolism—A subset (about 7%) of the population has reduced activity of the drug metabolizing enzyme cytochrome PA450IID6. Such individuals are referred to as

Continued on next page

This product information was prepared in June 1995. Current information on these and other products of Dista Products Company may be obtained by direct inquiry to Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, Indiana 46285, (800) 545-5979.